

CLASSIFICATION SECRET **SECRET**CENTRAL INTELLIGENCE AGENCY  
INFORMATION FROM  
FOREIGN DOCUMENTS OR RADIO BROADCASTS CD NO.

REPORT

COUNTRY USSR

SUBJECT Medical - Nerve stimulants

HOW PUBLISHED Thrice-monthly Periodical

WHERE PUBLISHED Moscow

DATE PUBLISHED Apr 1948

LANGUAGE Russian

DATE OF INFORMATION 1948.

DATE DIST. 26 Aug 1949

NO. OF PAGES 5

SUPPLEMENT TO REPORT NO.

50X1-HUM

THIS DOCUMENT CONTAINS INFORMATION AFFECTING THE NATIONAL DEFENSE OF THE UNITED STATES WITHIN THE MEANING OF ESPIONAGE ACT 50 U.S.C. 91 AND 92, AS AMENDED. ITS TRANSMISSION OR THE REVELATION OF ITS CONTENTS IN ANY MANNER TO AN UNAUTHORIZED PERSON IS PROHIBITED BY LAW. REPRODUCTION OF THIS FORM IS PROHIBITED.

THIS IS UNEVALUATED INFORMATION

SOURCE Doklady Akademii Nauk, SSSR, Vol LX, No 3, 1948.  
(PDB Per Abs 77T71 -- Information requested.)

ACTION OF PHENAMINE ON CONDITIONED  
MOTOR REFLEXES IN MONKEYS

L. G. Voronin, G. I. Shirkova  
Sumsk Biological Sta  
Acad Med Sci USSR

It is known that phenamine, a synthetic alkaloid belonging to the class of sympathicotropic alkaloids, stimulates the activity of the central nervous system, prevents sleep, and eliminates fatigue and the sleep condition. A number of clinical and experimental researches have been devoted to the study of the action of this drug on the organism.

According to the data of A. A. Volokhov and L. T. Zagorul'ko (1), A. I. Kuznetsov (3), and many others, phenamine acts upon the upper sections of the brain (the cortex and subcortex formations). It does not always produce a positive effect, however; in certain cases (10 - 15 percent), the administration of phenamine causes opposite phenomena, i.e., deterioration of the state of health, rapid fatigue, pain in the region of the heart, loss of appetite, etc. (1 - 3). According to the objective indications of these tests, it is possible to conclude that phenamine in doses of 0.015 - 0.02 gram increases the tone of the cortex of the dominant hemisphere. The experiments of A. I. Kotlyarevskiy (4) on animals and V. K. Faddeyeva (5) on children, using the method of conditioned reflexes, confirm this assumption. Faddeyeva observed that optimal doses of phenamine (0.0025 and 0.005 gram in children 8 to 12 years old) shortened the latent period of conditioned motor reflexes and increased the force of the reflex response, while differentiation was retained. Doses of 0.01 gram, while heightening the excitation process still further, inhibited differential and conditioned reflexes.

- 1 -

**SECRET**

CLASSIFICATION		SECRET		DISTRIBUTION									
STATE	<input checked="" type="checkbox"/> NAVY	<input checked="" type="checkbox"/> NSRB											
ARMY	<input checked="" type="checkbox"/> AIR	<input checked="" type="checkbox"/> FBI											

**SECRET**

SECRET

50X1-HUM

We conducted 28 experiments on conditioned reflexes in monkeys (Macaca lapunder) with phenamine in 50 cubic centimeters of milk administered 40 minutes before the experiment. Doses from 0.03 to 3 milligrams per kilogram weight of the animal were tested. Thus, the greatest dose was ten times greater than, and the smallest dose one tenth of, the therapeutic dose for humans.

The experiments on monkeys were conducted in their native habitats. The conditioned motor reflex was recorded by a push of the monkey's arm against a lever apparatus, placed before the cage, in response to a specific stimulus. The experimenter was shielded from the monkey by a board containing a panel for controlling the feeding trough and conditioning signals. A set consisting of a metronome, a bell, and the light of a 40-watt electric light bulb was used as the specific stimulus. A set consisting of a metronome or a different frequency, a siren, and the light of a 40-watt red electric light bulb was used as a differential. The positive set was used nine times, and the differential set three times during the experiment.

In response to the action of the specific stimulus, the monkey usually ran to the apparatus, pushed the lever, picked up the pieces of food falling into the trough, and then left. The latent period of the conditioned reflex was usually 1 - 3 seconds. The action of the stimulus, the conditioned reflex, and their duration were registered by a pneumatic transmission to the smoked tape of a kymograph; in addition, the experimenter recorded the proceedings of the experiment in detail.

Two 12-year-old monkeys, Zyuzya and Nal'ma, were experimented upon, the former being more excitable than the latter. Signs of excitation usually appeared 30 - 40 minutes after the phenamine was administered; thus the animals scratched themselves, moved about from place to place, and imitated the threats of the experimenter. These phenomena were most markedly expressed (especially in Nal'ma) after a 3 milligram per kilogram dose. The monkeys shrieked, looked in the window, climbed along the cage screening, etc. Even when Nal'ma showed absolutely no reaction to the specific stimulus on the apparatus, she would not always take the food thrown into the trough. The same unfavorable repressive action on the specific stimulus was observed even after a dose of 0.18 milligram. Both the first and the second doses repressed the conditioned reflexes for 24 hours, and even on the second day the monkeys did not respond to the conditioned signal of certain combinations. Thus, the dose used for humans proved unfavorable for monkeys. A dose of 0.12 milligram did not show any special influence on the conditioned-reflex response with the exception that the general excitation and latent period of all nine conditioned reflexes manifested during the experiment was increased (not exceeding one second). The duration of the reaction was also reduced somewhat. Obviously this dose ( $2\frac{1}{2}$  times less than that for humans) was the optimal one for these monkeys. The experiments described were conducted in the morning, in the usual working hours with monkeys.

One of us (G. I. Shirkova) had noted previously that monkeys have a clearly expressed daily periodicity in their conditioned-reflex activity. It is known that monkeys go to sleep with the approach of darkness and sleep until dawn. It has been shown that their conditioned-reflex response is disturbed throughout the night, from 2100 to 0800. A monkey awakened in the period from 2100 until 0100 yawns, is very sluggish, and reacts positively to only part of the stimulus, i.e., he takes the food and eats; the same holds true

- 2 -

SECRET

**SECRET**

**SECRET**

SECRET

50X1-HUM

in the period from 0500 to 0800. In the interval between 0100 and 0500, the monkey shows no reaction to the specific stimulus or turns away from it. This phenomena was established by a series of experiments on Zyuzya and Nal'ma at different hours of the day.

We decided to test the action of phenamine in this "dead" period. A light was lit in the compartment before the experiment, the monkeys were given phenamine, the light was turned off, and the monkeys left alone. After 40 - 50 minutes, the monkeys usually remained awake and exhibited the previously described motor excitation.

The curve describing the dynamics of the conditioned motor reflexes (in percent) with respect to the total number of specific stimuli during the experiment are shown in the appended graph. The curve was constructed from data obtained in an experiment on Zyuzya. A similar curve could have been constructed from experiments on Nal'ma. As seen in the graph, the conditioned reflexes are absent from 0100 to 0500. In this time interval, we tested the following phenamine doses on each monkey: 0.06, 0.09, 0.12, 0.18, 0.3, 1.2, 1.8, and 2.4 milligrams per kilogram weight. The percent of positive reactions is denoted by a dot for Zyuzya and by a triangle for Nal'ma.

In the period of deep sleep, as shown, phenamine in doses from 0.06 to 1.2 milligrams exhibits a varying positive action, removing the sleep condition. Moreover, the conditioned-reflex response of one monkey, Zyuzya, was fully restored after a 0.06 milligram dose, i.e., one fifth that used for humans. Doses approximating, or equal to, that used in humans caused a less positive effect, as is shown by the fact that the monkeys reacted only partially to the stimulus. In all cases, the positive action of phenamine on conditioned reflexes in Nal'ma was less than in Zyuzya, but the general motor excitation was more strongly expressed. The larger doses of 1.8 and 2.4 milligrams, i.e., doses six to eight times greater than that used in humans, caused depression of the motor reflexes and exceedingly strong motor excitation; the monkeys screamed loudly and picked at their fur. In all these tests, the phenamine action lasted over 24 hours. In a number of cases (in seven of 28), a differential recurrence was observed 5 - 6 hours after administering phenamine, but in the majority the conditioned-reflex response gradually returned to normal in 24 hours. The repressive action of phenamine remained for 48 hours for the larger doses.

These tests were conducted over a period of 7 months. Phenamine was administered not more than once a week, but nonetheless, lack of appetite and general malaise were noted in early January 1948. Zyuzya, originally weighing 7,300 grams, lost 1,200 grams, while Nal'ma, originally weighing 7,700 grams, lost 1,700 grams. Since such a large loss in weight was not observed previously in these monkeys, we discontinued further tests.

Thus, we investigated the action of phenamine only in the morning hours, when the monkeys were in the most active state, and in the evening hours, when they were in deep sleep.

The results of the experiments established that:

1. The optimal dose of phenamine per kilogram of weight in monkeys is considerably less (one quarter to one fifth) than the optimal dose in humans.

- 3 -

SECRET

**SECRET**

50X1-HUM

**SECRET**

SECRET

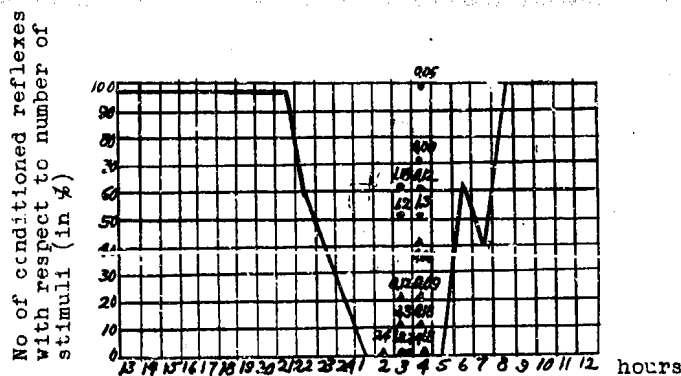
2. In the morning hours, small doses do not cause a noticeable effect upon conditioned reflexes, but large doses act repressively, obviously due to the negative action of the general motor excitation present at this time.

3. In the period of deep sleep in the evening, doses from 0.06 to 0.12 milligram per kilogram weight remove the sleep condition, while larger doses (from 1.6 to 2.4 milligrams) cause strong motor excitation with a complete absence of conditioned-reflex response.

4. The repressive action of phenamine on conditioned reflexes lasts from 24 to 48 hours.

5. The systematic use of phenamine, especially in large doses, causes loss of appetite and a sharp drop in weight in monkeys.

We will study the action of phenamine at different times of day (when the monkeys are falling asleep and when they are waking up) on other monkeys because of the reasons mentioned previously.



• No of conditioned reflexes in experiment with phenamine on Zyuzya

▲ Same as above, for Nall'ma

Numbers over the dots and triangles are the phenamine doses in milligrams per kilogram weight of the monkey

- 4 -

SECRET

**SECRET**

**SECRET**

SECRET

50X1-HUM

Bibliography

1. A. A. Volokhov and L. T. Zagorul'ko, Voen.-Med. Sb., 1, 81, 91, 98 (1944)
2. A. G. Ginetsinskiy, Ya. F. Samter, and N. V. Natanson, Voen.-Med. Sb., 1, 75 (1944)
3. A. I. Kuznetsov, Tr. Voen.-Med. Akad., 1, 187 (1946)
4. A. I. Kctlyarevskiy, Refer. N.-I. Rab. Akad. Med. Nauk, 76 (1947)
5. V. K. Faddeyeva, Refer. N.-I. Rab. Akad. Med. Nauk, 157 (1947)

- E N D -

- 5 -

SECRET

**SECRET**